

What is claimed is:

- 1) A composition comprising gp120 and a nucleic acid aptamer that binds to gp120 and induces gp120 to undergo a conformational shift whereby an epitope to a membrane bound receptor is exposed that is capable of eliciting a humoral immune response.
- 2) The composition of Claim 1 wherein the epitope to the membrane bound receptor is an epitope to CCR5.
- 3) The composition of Claim 1 wherein the epitope to the membrane bound receptor is an epitope to CXCR4.
- 4) The composition of Claim 1, 2 or 3 wherein the nucleic acid aptamer is selected from SEQ ID No. 9 through SEQ ID No. 225.
- 5) A method of vaccinating a subject against HIV infection comprising administering to a subject a composition comprising gp120 and a nucleic acid aptamer that binds to and induces gp120 to undergo a conformational shift whereby an epitope to a membrane bound receptor is exposed that is capable of eliciting a humoral immune response.
- 6) The method of Claim 5 wherein the epitope to the membrane bound receptor is an epitope to CCR5.
- 7) The method of Claim 5 wherein the epitope to the membrane bound receptor is an epitope to CXCR4.
- 8) The method of claim 5, 6 or 7 wherein said nucleic acid aptamer is selected from SEQ ID No. 9 through SEQ ID No. 225.
- 9) A method of producing neutralizing antibodies specific to gp120 comprising administering a composition comprising gp120 and a nucleic acid aptamer that binds to gp120 and induces gp120 to undergo a conformational change whereby an epitopes to a membrane bound receptor is exposed that is capable of eliciting a humoral immune response.

- 10) The method of Claim 9 wherein the epitope to the membrane bound receptor is an epitope to CCR5.
- 11) The method of Claim 9 wherein the epitope to the membrane bound receptor is an epitope to CXCR4.
- 12) The method of claim 9, 10 or 11 wherein said nucleic acid aptamer is selected from SEQ ID No. 9 through SEQ ID No. 225.
- 13) The method of Claim 9 wherein neutralizing antibodies are produced.
- 14) A method of treating HIV infection comprising the step of administering a composition comprising gp120 and a nucleic acid aptamer that binds to gp120 and induces gp120 to undergo a conformational change whereby an epitope to a membrane bound receptor is exposed that is capable of eliciting a humoral immune response.
- 15) The method of Claim 14 wherein the epitope to the membrane bound receptor is an epitope to CCR5.
- 16) The method of Claim 14 wherein the epitope to the membrane bound receptor is an epitope to CXCR4.
- 17) The method of claim 14, 15 or 16 wherein said nucleic acid aptamer is selected from SEQ ID No. 9 through SEQ ID No. 225.
- 18) An aptamer that binds to gp120 selected from SEQ ID No. 9 through SEQ ID No. 225.
- 19) A composition comprising an aptamer that binds to gp120 selected from SEQ ID No. 9 through SEQ ID No. 225.
- 20) An aptamer that binds to gp120 complexed to gp120, wherein said aptamer is selected from SEQ ID No. 9 through SEQ ID No. 225.

- 21) A method of treating HIV infection in a subject comprising administering a therapeutically effective amount of an aptamer that binds gp120 selected from SEQ ID No. 9 through SEQ ID No. 225.
- 22) A method of treating HIV infection in a subject comprising administering a therapeutically effective amount of an aptamer that binds to gp120 complexed to gp120, wherein said aptamer is selected from SEQ ID No. 9 through SEQ ID No. 225.
- 23) A method of preventing HIV infection in a subject comprising administering a prophylactically effective amount of an aptamer that binds to gp120 complexed to gp120, wherein said aptamer is selected from SEQ ID No. 9 through SEQ ID No. 225.
- 24) A method of producing neutralizing antibodies with specificity to HIV gp120 comprising administering an aptamer that binds to gp120 complexed to gp120, wherein said aptamer is selected from SEQ ID No. 9 through SEQ ID No. 225.
- 25) A method of eliciting a humoral immune response in a subject resulting in neutralizing antibodies specific gp120 comprising administering an aptamer that binds to gp120 complexed to gp120, wherein said aptamer is selected from SEQ ID No. 9 through SEQ ID No. 225.
- 26) A method for identifying an aptamer that binds to gp120 and induces gp120 to undergo a conformational change whereby an epitope to a membrane bound receptor is exposed that is capable of eliciting a humoral immune response comprising the steps of:
- (a) synthesizing aptamers with spacers from about 20 to about 200 Angstrom spacers ending in a primary amine moiety;
 - (b) generating single free thiols on cysteine mutations in the N termini, C termini and/or the non-neutralizing face of gp120;
 - (c) covalently attaching said aptamers with a crosslinker to said free thiols on gp120; and
 - (d) screening aptamers for binding to a gp120 epitope.

- 27) A method for identifying an aptamer that binds to gp120 and induces gp120 to undergo a conformational change whereby an epitope to a membrane bound receptor is exposed that is capable of eliciting a humoral immune response comprising the steps of:
- (a) synthesizing aptamers with spacers from about 20 to about 200 Angstrom spacers ending in a primary amine moiety;
 - (b) generating single free thiols on cysteine mutations in an antibody or antibody fragment that binds to gp120;
 - (c) covalently attaching said aptamers with a crosslinker to said free thiols on the antibody or antibody fragment; and
 - (d) screening aptamers for binding to a gp120 epitope.
- 28) The method of Claim 26 or 27 wherein said spacer is polyethylene glycol.
- 29) The method of Claim 26 or 27 wherein said crosslinker is a hetero-bifunctional crosslinker
- 30) The method of Claim 29 wherein said hetero-bifunctional crosslinker is Sulfo-LC-SPDP (sulfosuccinimidyl 6-[3'-(2-pyridyldithio)-propionamido] hexanoate).
- 31) The method of Claim 30 wherein said gp120 epitope is selected from CCR5 and CXCR4.
- 32) The method of Claim 26 or 27 wherein said screening is performed with gp120 BaL mutants and said screening is performed with CCR5 peptides or full CCR5 receptor.
- 33) An aptamer comprising a first binding domain which recognizes a first ligand coupled to a second binding domain which recognizes a second ligand wherein binding of the second ligand by the second binding domain is regulated by binding of the first ligand by the first binding domain.
- 34) The aptamer of Claim 33, wherein the first ligand binding domain specifically interacts with an allosteric effector molecule and the second ligand binding domain specifically interacts with a target of the allosteric effector molecule.

- 35) The aptamer of Claim 34, wherein the allosteric effector molecule is gp120 and the target is the CCR5 receptor.
- 36) The aptamer of Claim 33, wherein binding of the second ligand by the second binding domain is activated by binding of the first ligand by the first binding domain.
- 37) The aptamer of Claim 34, wherein binding of the second ligand by the second binding domain is activated by binding of the first ligand by the first binding domain.
- 38) The aptamer of Claim 33, wherein binding of the second ligand by the second binding domain is suppressed by binding of the first ligand by the first binding domain.
- 39) The aptamer of Claim 34, wherein binding of the second ligand by the second binding domain is suppressed by binding of the first ligand by the first binding domain.
- 40) A method of selecting regulated aptamers comprising the steps of isolating first and second aptamers which bind first and second ligands, respectively, using SELEX, engineering a diverse sequence pool of molecules that contain the binding domains of the first and second aptamers, and selecting for regulated aptamers from that pool wherein binding of the second ligand by the second binding domain is regulated by binding of the first ligand by the first binding domain.
- 41) A method of treating HIV in a subject comprising the steps of administering a therapeutically effective amount of an CCR5 receptor aptamer, wherein said CCR5 receptor aptamer binds to a gp120 effector and is activated by the gp120 effector to bind to said CCR5 receptor, and preventing gp120 binding to cells.